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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,686	12/10/2003	Yaron Ilan	59046.000043 Enz-64(D2)	9035

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/22/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,686	ILAN ET AL.	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/22/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,40-42,45-49,63 and 64* is/are pending in the application.

4a) Of the above claim(s) *46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37, 40-42, 45, 47-49 and 63-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-36, 38-39, 43-44 and 50-62 are cancelled. Claims 37, 40-42, 45-49 and 63-64 are pending. Claim 46 is withdrawn from consideration because it is not drawn to the elected invention, which is HCV. Claims 37, 40-42, 45, 47-49 and 63-64 are under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 37, 40-42, 45, 47-49 and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al.,[1] in view of Motoki et al.,[2] in further view of Lin et al.[3]

In response to the rejection, Applicant argues that claimed invention is not obvious over the cited references. Applicant submits that none of the references teaches of a "mammalian intermediary metabolite". Turning to Motoki et al., Applicant argues that the compounds described by Motoki et al. are not mammalian intermediary metabolites as they are not synthesized compounds that are not found in nature.

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[1] Ogawa et al. U.S. Patent No. 5861520, published January 19, 1999.
[2] Motoki et al. Immunostimulatory and antitumor activities of monoglycosylceramides having various sugar moieties. Biol. Pharm. Bull., November 1995, Vol. 18, No. 11, 1487-1491.
[3] Lin et al. U.S. Patent No. 6043339, published March 28, 2000.

Regarding Ogawa et al., Applicant argues that the reference does not describe mammalian intermediary metabolite. Applicant also notes that all the experiments disclosed by Ogawa et al. incorporate the use of artificial or non-natural glycolipids rather than natural glycolipids. And, turning to Lin et al., Applicant argues that Lin et al. does not disclose the compounds of the present invention. Without a teaching of the compounds, the combination of the cited references does not result in the claimed method. That is, Applicant submits that there is no motivation to combine the references and there would be no expectation of success.

Applicant's arguments have been considered, however, it is not found persuasive. Regarding Motoki et al., Motoki et al. teaches of beta-glucosylceramide and beta-galactosylceramide. According to Applicant's disclosure, paragraph 0006, alpha-glucosylcerebroside is a compound that is isolated from a marine sponge and is not a compound normally found in mammalian cells. Since there are only two possible configurations (alpha or beta) for linking a sugar to a ceramide exists, a glucosylceramide that is not an alpha glucosylceramide is a beta-glucosylceramide. This argument is further substantiated by the 01/22/2010 submission made by Applicant in the parent patent application, 10/375906. In said submission, Applicant clearly details that the compounds encompassed by the claimed invention are beta-glucosylceramide and beta-galactosylceramide. In the instant case, since Motoki et al. teaches of beta-glucosylceramide and beta-galactosylceramide, and Applicant's claimed invention encompasses both compounds, Applicant's argument is not found persuasive.

Regarding the Ogawa et al., at lines 35-50, column 1, Ogawa et al. teaches of mammalian intermediary metabolites. The mammalian intermediary metabolites that Ogawa et al. teaches are beta-glucosylceramide and beta-galactosylceramide.

Regarding the teachings of Lin et al., while it is noted that Lin et al. does not teach a mammalian intermediary metabolite, however, the teachings of Lin et al. is relevant for Lin et al. establishes that glycolipids may be administered using an ex vivo process, as claimed. Lin et al. is cited to compensate the deficiencies noted in Ogawa et al. and Motoki et al. In the instant case, Lin et al. fully compensates for the noted deficiencies.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, the motivation to combine the cited references is clearly detailed in the rejection.

Both Ogawa et al. and Motoki et al. teach of glycolipids. Both references disclose of the sphingoid polyalkylamine conjugates recited in Applicant's claims. Ogawa et al. teaches that glycolipids, including the conjugate recited in the claims, closely relate to receptor functions for physiologically active substances and important cell functions,

such as generation, proliferation, differentiation or immune reactions, via intercellular recognition and interactions. Ogawa et al. also establishes that it is known that glycolipids play a role as a receptor in the host side in the infection with bacteria and viruses. [Lines 55-61, column 1, in particular.] Based on this knowledge, Ogawa et al. discloses the use of glycolipids to inhibit viral infections. Thus, at the time the invention was made, Ogawa et al. establishes that glycolipids have antiviral activities. Additionally, Motoki et al. establishes that the conjugate recited in the claims is immunostimulatory. In the instant case, the Motoki et al. clearly teaches the administration of the conjugate to induce an immune response. Combining the teachings of Motoki et al. and Ogawa et al., one of ordinary skill in the art, at the time the invention was made would be motivated to administer the conjugate to a virally infected subject to inhibit viral infection or to induce an immune response against the infection.

In the instant case, while neither reference teach an ex vivo method of administration of the desired glycolipid, however, Lin et al. establishes that at the time the invention was made, ex vivo administration methods are known and practiced in the art. Lin et al. further establish that glycolipids can be administered using the ex vivo method. Hence, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to administer the glycolipid of Motoki et al., using the process of Lin et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate delivery/administration of glycolipids to a subject. One of ordinary skill in the art, at the time the invention was

made would have had a reasonable expectation of success for doing so because Lin et al. clearly detail that glycolipids can be administered using the ex vivo process.

As previously presented, the claims are directed to a process comprising the active step of a) obtaining cells from a subject, b) treating said cells with an intermediary metabolite or a reagent that increases the intracellular level of a mammalian intermediary metabolite in said cells, and c) transferring said treated cells to said subject to a virally infected subject. Claim 40, which depends on claim 37, requires the glycolipid to comprise a monosaccharide ceramide, which is limited to glucosyl ceramide and galactosyl ceramide by claim 41. Claim 42, which depends on claim 37, requires the transferring step be carried by intravenous means. Claim 45, which depends on claim 37, requires the viral infection be HCV. Claim 47, which depends on claim 37, requires the reagent to increase the rate of production of said glycolipid in said subject. Claim 48, which depends on claim 37, requires the reagent to decrease the rate of degradation or turnover of said glycolipid in said subject. Claim 49, which depends on claim 37, requires the cells obtained from said subject to comprise peripheral blood monocytes (PBMCs), dendritic cells, T cells, stem cells, NK cells, NKT cells and CD1d cells. Claims 63-64, which depend on claims 40-41, respectively, require the viral infection to be HCV.

Motoki et al. teaches of glycolipids. The glycolipids of Motoki et al. are monosaccharide ceramide, including beta-glucosylceramide and beta-galactosylceramide. Motoki et al. teaches the administration, subcutaneous, of beta-glucosylceramide and beta-galactosylceramide to a subject.

The subject of Motoki et al. is not a virally infected subject, including humans. However, at the time the invention was made, Ogawa et al. also teaches that glycolipids, including beta anomers of the glucosylceramide and galactosylceramides closely relates to receptor functions for physiologically active substances and important cell functions, such as generation, proliferation, differentiation or immune reactions, via intercellular recognition and interactions. Ogawa et al. also establishes that it is known that glycolipids play a role as a receptor in the host side in the infection with bacteria and viruses. [Lines 55-61, column 1, in particular.]Based on this knowledge, Ogawa et al. discloses the use of glycolipids to inhibit viral infections. Thus, at the time the invention was made, Ogawa et al. establishes that glycolipids have antiviral activities.

Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to administer the glycolipids taught by Motoki et al. to a virally infected subject, including human and those infected with HBV, HCV or HIV. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to inhibit viral infection or to induce an immune response against the infection. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the antiviral activities of glycolipids has been demonstrated and established by Ogawa et al.

Neither Ogawa et al. nor Motoki et al. teach an ex vivo method of administration of the glycolipid. However, at the time the invention was made, Lin et al. teaches a process comprising the active step of a) obtaining cells from a subject, b) treating said cells with reagent, and c) transferring, intravenously said treated cells to said subject.

Lin et al. also notes that the process can be used to deliver glycolipids. [Lines 37-46, column 2, in particular.] Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to administer the glycolipid of Motoki et al. using the process of Lin et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to import facilitate delivery/administration of glycolipids to a subject. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because Lin et al. teaches that glycolipids can be administered using the administration process disclosed by Lin et al.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on (571) 272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner, Art Unit 1648

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